PERSPECTIVE

The Patient-Centered Future of Clinical Pharmacology

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Over the past decade, we have witnessed remarkable technological progress, advances in drug discovery, development, and regulation, as well as changes toward value-based and personalized health care. These changes provide unprecedented opportunities for innovation and focusing on patients in ways that have not happened before. Herein, we share our views about the future of clinical pharmacology and the opportunities and challenges of moving the field toward patient-centric clinical pharmacology and personalized medicine.

Today, clinical pharmacologists are well positioned to drive advancements in precision medicine and shape the future of the clinical pharmacology field to impact patients' lives more than ever before. We are now observing large-scale changes (**Figure 1**) driven by technological advancements that will provide transformational opportunities for driving patient-centric clinical pharmacology and improving patient outcomes.

DIGITIZATION OF PATIENT CARE

Electronic health records

The continued growth in the volume and variety of data and the fast-paced digitization of patient care with electronic health records (EHRs) are substantial changes that provide clinical pharmacologists with unprecedented avenues for innovation in drug development and improving patient care. We are witnessing widespread adoption of EHRs with more than 95% of US hospitals having certified EHR technology.[1] Additionally, efforts to merge patient genomics data and specimens with EHR data are underway. For instance, National Institutes of Health (NIH)–funded programs such as eMERGE (Electronic Medical Records and Genomics; https://emerge.mc.vanderbilt.edu/) and IGNITE (Implementing Genomics In Practice; www.ignite-genomics.org) were established to support the integration of genomics data to patient data in EHRs and the development of tools for point-of-care decision making. As clinical pharmacologists, we have an opportunity to improve patient care via EHR by implementing decision support tools that can provide accurate and timely therapeutic intervention and more effective individualized therapies with a minimized risk for adverse events. We can utilize the longitudinal data in EHRs to identify novel biomarkers of drug response and model disease progression. Additionally, we can leverage EHR data to study participants not represented in phase III clinical trials and generate evidence for regulatory and clinical decision making. Leveraging EHR data during clinical trials can help in streamlining data collection and accurately capture safety and efficacy end points. For instance, during a clinical trial, some patients may accidentally forget to report adverse events; however, if the EHR data are integrated during the clinical trial, then we can capture such events.

Despite the advantages that the EHR offers for empowering patient-centric clinical pharmacology implementation, leveraging EHR data comes with several challenges that need to be addressed. For example, there are concerns related to data security and privacy, handling and analyzing EHR data, along with data standardization and interoperability between different EHRs in different health systems.[2] We need to continue establishing collaborative networks with data scientists and informaticists to ensure development of a proper infrastructure to handle and analyze EHR data and ensure strong privacy protection to patients. As a scientific community, we need to explore newly emerging legal and technical tools to evaluate and mitigate any risk that may affect the patient's privacy. We also need to continue investing in the new wave of clinical pharmacologists who may be interested in developing decision support tools in the EHR and leveraging EHR data to inform drug development and decision making in healthcare settings.

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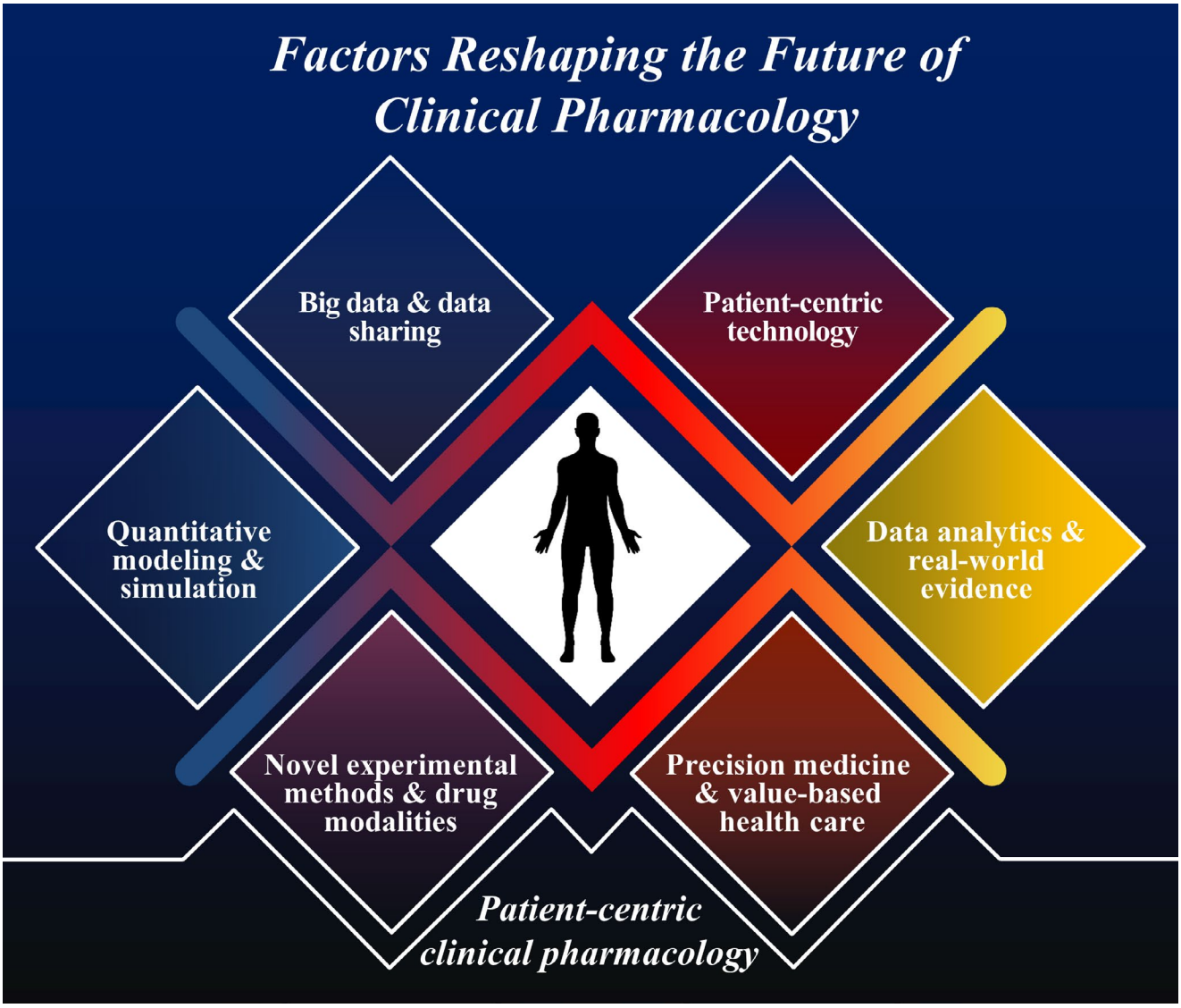

Figure 1 Factors transforming the field of clinical pharmacology.

Digital technology

The evolution of digital technology, such as wearables or adherence-measuring techniques, offers an opportunity to continuously monitor patients in ways that were not available before. We can closely monitor patients outside the clinic and efficiently collect patient data in real time. With the rapid advancement in digital technology, clinical pharmacologists have increased opportunities to use this technology to monitor patient response to therapeutic interventions more closely and generate real-world evidence for making informed decisions. We have already witnessed the impact of real-world evidence in driving regulatory decisions[3] and, in the near future, we expect greater endorsement and utilization of evidence generated from real-world data in driving individualized clinical decisions and informing drug development.

Despite the benefits expected from using wearables and digital sensors in driving patient-centric clinical care, privacy and security of data generated from these sources represent a challenge. Additionally, technical issues exist for integrating and analyzing the heterogeneous data generated from these tools. To overcome these challenges, more collaboration between academia, industry, regulatory bodies, policymakers, and patients is critical to assess the benefit–risk associated with using real-world data from wearables and digital sensors. We need technological solutions that include proper privacy and security controls. We should guarantee that mechanistic inferences drawn from real-world data are robust and reproducible. We also need innovative data management platforms that enable large, heterogeneous data sets to be structured, stored, and analyzed. New approaches and methodologies for data interrogation and research to facilitate decoding data generated from wearables to improve patient care are also important.

DATA SHARING

Today, sharing data, workflows, and methods is more important for the progress of our field than ever, as it will help drive novel insight into drug discovery and development that is both robust and reproducible. Sharing data from clinical

research and clinical trials will empower clinical pharmacologists to make informed clinical care decisions and improve patients' outcomes by producing better evidence on the efficacy and safety of drugs via the application of model-informed drug development and conducting a well-powered meta-analysis. There are continuous efforts to increase transparency and overcome the challenges of sharing clinical research data between academia, industry, regulatory agencies, and patients. Patients increasingly request enhanced clinical trial transparency and access to their health data and clinical trial results.[4] Patient advocates in disease areas like Parkinson's, where there is a lack of effective treatment, are advocating for sharing their own data with research organizations to maximize the value of clinical trial research and help discover effective therapeutic breakthroughs for their diseases.[5] Reusing clinical trial data shared in areas like Parkinson's (Parkinson's Progression Markers Initiative; https://www.ppmi-info.org/), oncology (Data Sphere Project; https://www.projectdatasphere.org/projectdatasphere/html/home), and immunology (ImmPort; https://www.immport.org/home) helped in identifying novel biomarkers associated with disease progression and variability in drug response. These biomarkers hold the promise of improving clinical care decisions for patients with those debilitating diseases.[6–8]

Clinical pharmacologists are well positioned to pave the way for clinical data sharing within institutions and research communities to expedite the drug development process. We must continue working on behalf of patients to incentivize data sharing, develop data-sharing plans within clinical study protocols, and demonstrate how sharing clinical data can help expedite drug development programs and address patients' unmet needs. We must continue educating current and future generations of clinical pharmacologists to become more patient-centric and adapt to ever-evolving patient needs during drug development and patient care.[9]

EXPERIMENTAL AND QUANTITATIVE METHODS

Current advances in omics profiling, biomarker discovery, and the evolution of experimental approaches, including human induced pluripotent stem cells and human brain organoids, provide unprecedented opportunities to bridge the gap between basic science and clinical research. Additionally, the rise of model-informed drug development (MIDD) approaches has paved the way for quantitative systems pharmacology and physiologically based models to increase the confidence in decision making across the drug development continuum. These quantitative systems approaches are now used to integrate current knowledge about the drug, disease, and mechanism of action, and allow the prediction of outcomes under untested conditions. Additionally, advances in machine-learning applications have shown potential in improving data-driven decision making by exploiting big data to provide clinical benefit. Although advances in machine learning hold promise to reinvigorate the clinical pharmacology data analysis framework, we do not think this will replace conventional approaches. We believe the real promise of machine learning lies in the combination with traditional modeling and simulation approaches to make faster and more informed decisions.

As clinical pharmacologists, we have a great opportunity to enhance our role as the conduits of translation between basic and clinical research and overcome barriers that impede the translation of new knowledge from the bench to the clinic and back to the bench. We must support data collaboration and translational modeling and simulation activities to develop an integrated system that includes different types of data (pharmacokinetic, pharmacodynamic, pharmacogenomic, pharmacoeconomic, biomarkers, activity data) with high translational and predictive power to improve patient care and reverse the endless series of failed clinical trials. In parallel, we must train and engage clinical pharmacologists to use the essential tools that will equip them to bridge the translational chasm between basic science and clinical research and improve patient care by translating clinical research into practice.[9]

MODALITY DIVERSIFICATION

Recent years have seen an explosion in the discovery and development of novel therapeutic modalities. Historically, clinical pharmacology dealt with small molecule drugs. More recently, therapeutic antibodies became an important modality, and clinical pharmacology adjusted its practices. It is becoming routine to think about clinical pharmacology approaches to support the development of small molecules, antibodies, bispecifics, antibody–drug conjugates, vaccines, peptides, protein replacement, RNA therapeutics, gene therapy, gene editing, and cell therapy. Regardless of the modality, the core clinical pharmacology principles, like dose-finding and characterization of exposure–response, will remain pivotal, and it is critical for clinical pharmacologists to continue to explore where these novel therapeutics require new paradigms in the drug development and use processes.

FINAL REMARKS

The ultimate goal of clinical pharmacology is to deliver the right drug to the right patient with the right dose at the right time. As we look toward the future, this objective will not change, but we will live by this mantra in unprecedented ways. The use of pharmacometrics, pharmacogenomics, and new quantitative tools to inform and optimize the drug development process and clinical care decisions will continue to be critical. As healthcare delivery begins the shift towards value-based models[10] that incentivize systems to provide improved care at lower costs, clinical pharmacology-based tools that make the provision of care more efficient and effective will be highly sought after.

As big data continue to get bigger and more diverse, our toolbox will need to adopt new methods to handle this data deluge. However, regardless of how sophisticated our toolbox will be in the future, clinical pharmacologists must learn to simplify and integrate key messages and speak with one voice to various audiences. We also believe that the role of MIDD is anticipated to go beyond decision making within a pharmaceutical company to a regulatory agency's assessment of the benefit/risk ratio through the US Food and Drug Administration's (FDA's) MIDD pilot programs under the Prescription Drug User Fee Act (PDUFA) VI. Model-informed clinical endpoints that are reliable early surrogates of longer-term clinical outcomes

could facilitate earlier global access to new therapies and transform clinical practice, particularly where value-based pricing is adopted.

In conclusion, as a diverse scientific community, we must work together to realize the potential clinical pharmacology holds to improve the health and well-being of humankind. We must open our doors for multidisciplinary collaborations and sharing data, workflows, and methods to successfully bridge the translational gap between basic science and clinical research and improve the reproducibility of our discoveries. We must also embrace each other with a unifying goal, which is to act on behalf of our patients and develop meaningful solutions to their unmet medical needs.

CONFLICT OF INTEREST

M.H.S. is an employee of Pfizer Inc.; J.A.W. is an employee of Foresite Capital; K.M.M. is an employee of Genentech Inc.; and J.A.J. serves as a consultant for United Health Group. The other authors declared no conflict of interest.

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